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Selenium biomarkers and miR-7-5p in overweight/obese women

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ABSTRACT

Introduction: Chronic low-grade inflammation and oxidative stress are pivotal contributors to the metabolic complications associated with obesity. Selenoprotein P (SELENOP) and glutathione peroxidase 1 (GPx1) are selenoproteins involved in the reduction of reactive oxygen species and pro-inflammatory cytokines levels. Nutritional epigenomics revealed the interaction of microRNAs and nutrients with an important impact on metabolic pathways involved in obesity. However, the knowledge regarding the influence of microRNA on selenium biomarkers and its impact on metabolic pathways related to obesity remains scarce. Thus, the aim of this study was to investigate the association of plasma miR-7-5p expression with selenium and inflammatory biomarkers in women with overweight/obesity.

Material and methods: Anthropometric evaluations were performed and blood samples were collected for the analysis of fasting glucose, insulin, inflammatory and selenium biomarkers, and miR-7–5p expression in 54

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women with overweight/obesity. Gene expression of *SELENOP* and *GPX1* were evaluated in peripheral mononuclear blood cells.
Results: This study observed a negative correlation between SELENOP levels and miR-7–5p (rho = −0.350; p = 0.018). Additionally, it was observed that body fat (OR = 0.737; p = 0.011), age (OR = 1.214; p = 0.007), and miR-7-5p (OR = 0.990; p = 0.015) emerged as significant predictors of SELENOP levels.
Conclusions: In conclusion, we observed a significant inverse association between miR-7-5p expression and SELENOP concentration in overweight/obese women, suggesting that age and percentage of body fat are also associated.
Trial registration number: Brazilian Registry of Clinical Trials (ReBEC) number RBR-2nfy5q

1. Introduction

Overweight and obesity are prevalent worldwide and are characterized by an excess of adipose tissue that results in a state of low-grade chronic metabolic inflammation, able to increase the risk of type 2 diabetes (T2D) and cardiovascular diseases. Nutrients with anti-inflammatory and antioxidant properties play a crucial role in managing metabolic disorders [1].

Selenium (Se) is an essential trace element that influences inflammation and oxidative stress through selenoproteins like Glutathione peroxidase 1 (GPx1) and selenoprotein P (SELENOP) [2]. GPx1 reduces hydrogen peroxide, thereby attenuating inflammation, which is elevated in obesity. SELENOP, responsible for selenium transport and antioxidant defense, is associated with insulin resistance, carbohydrate metabolism and visceral obesity [3].

Nutritional genomics, particularly Nutrimiromics, explores how diet and nutrients influence gene expression. Studies suggest that microRNAs (miRNAs) play a significant role in metabolic disorders and can be regulated by selenium status [4]. For example, miR-7-5p is linked to SELENOP levels and its expression is down regulated in patients with T2D [5,6]. However, there is a need for results that clarify the association between miR-7-5p and selenium biomarkers, particularly in overweight and obese populations. A meta-analysis indicated that miR-7-5p levels were upregulated in individuals with obesity post-bariatric surgery [7]. Thus, this study aims to further elucidate the influence of metabolic inflammation on this relationship.

This study seeks to contribute new insights to Nutrimiromics, shedding light on the interplay between miRNA regulation, Se status, and inflammation, which could inform future therapeutic strategies for managing metabolic complications in obesity. Thus, the aim of this study was to investigate the association of miR-7-5p with selenium biomarkers, gene expression and inflammatory parameters in women with overweight/obesity.

Table 1
Anthropometric and biochemical characteristics of the participants.

Variable (n=54)	Median (IQR)
Age (years)	41 (32.5 – 47.2)
Body fat (%)[a]	45.1 (41.5–50.8)
BMI (kg/m^2)	34.7 (31.9–37.7)
Fasting glucose (mg/dL)	83.0 (71.7–95.5)
Insulin (μU/mL)[b]	6.3 (3.3–9.7)
HOMA-IR	1.4 (1.0–2.9)
GPx1 activity (U/g Hb)	48.2 (40.8–57.7)
SELENOP (ng/mL)[c]	34.3 (11.3–51.9)
Plasma Se (μg/L)[c]	78.3 (64.6–90.8)
Erythrocyte Se (μg/L)	126.7 (114.4–147.1)
mRNA *GPX1* ($2^{-\Delta Ct}$)	0.2 (0.2–0.3)
mRNA *SELENOP* ($2^{-\Delta Ct}$ x 10^3)	0.1 (0.1–0.2)
IL−6 (pg/mL)	2.4 (1.3–3.4)
CRP (μg/mL)	10.9 (3.9–20.9)
TNF-α (pg/mL)	2.1 (1.5–2.8)
miR-7-5p ($2^{-\Delta Ct}$ x 10^3)	2.9 (2.1–4.1)

Legend: [a]2 missing values, [b]7 missing values, [c]9 missing values. Legend: GPx= glutathione peroxidase; IL-6= interleukin-6; IQR= Interquartile range; miR= microRNA; mRNA= messenger RNA (gene expression); Se= selenium; SELENOP= selenoprotein P; CRP=C-reactive protein; TNF-α= tumor necrosis factor alpha. Reference values: plasma Se - 60 a 120 μg/L; erythrocyte Se - 90 a 190 μg/L [15].

2. Material and methods

2.1. Population

This cross-sectional study exclusively used the baseline data from a randomized clinical trial (trial register: RBR-2nfy5q) that was conducted in the Division of Endocrinology and Metabolism at the Clinical Hospital (School of Medicine, University of São Paulo, Brasil). Fifty-four women aged between 18 and 60 years old, with a body mass index (BMI) ≥ 28.9 kg/m^2 according to Stern's criteria for diagnosing insulin resistance [8] were included. The inclusion criteria followed the original study [9]: women between 18 and 55 years of age, with a body mass index of 28.9–39.9 kg/m^2, not pregnant or participating in another clinical trial; not using vitamin-mineral supplements; not smoking or abusing alcohol; not engaging in intense physical activity; not allergic to nuts or reporting a regular consumption of Brazil nuts. The sample size calculation were previously described [9]. All the procedures involving the patients were conducted according to the guidelines laid out in the Declaration of Helsinki and approved by the Ethics Committee of the Faculty of Pharmaceutical Sciences at the University of São Paulo (approval number 1.421.929). Written informed consent was obtained from all participants.

2.2. Anthropometric assessment and blood samples collection

Body weight (kg) was measured using a calibrated digital scale and height (cm) by using a fixed stadiometer positioned on the scale [10]. Body mass index (BMI) was calculated (expressed as kg/m^2) and the classification was performed according to the World Health Organization (WHO) [11]. Body fat percentage (%BF) was determined using an electrical bioimpedance (InBody 770, Biospace, Seoul, Korea) according to the manufacturer's instructions.

Fasting blood samples (25 mL) were drawn by venipuncture using 5-mL EDTA tubes and 8-mL tubes without anticoagulant. Plasma and serum samples were separated by centrifugation at 3.000 g for 15 minutes at 4°C. Erythrocyte pellet obtained from whole blood was washed three times with 5 mL sterile 9 g/L NaCl solution, slowly homogenized by inversion and centrifuged at 10.000 g for 10 minutes at 4°C, and the supernatant was discarded. Plasma, serum, and erythrocyte aliquots were stored in free trace-elements polypropylene tubes at −80ºC until analysis was performed.

2.3. Biochemical analysis and insulin resistance evaluation

Fasting glucose was determined in serum samples using commercially available kit (Reference 84, Minas Gerais, Brazil) in an automated biochemical analysis (Labmax 240, Labtest, Minas Gerais, Brazil). The analysis of plasma inflammatory biomarkers (IL-6, TNF-α, C-reactive protein [CRP]) and insulin were performed by multiplex technique by using a commercial kit (Milliplex, Merck Millipore, Darmstadt, Germany). The homeostasis model assessment for insulin resistance

Table 2
Spearman's correlation of miR-7-5p and SELENOP with biochemical, anthropometric, and inflammatory biomarkers.

Variables	miR-7-5p (n=54)	SELENOP (n=45)
Age (years)	−0.046 [−0214; 0323]	0.281 [−0010; 0525]
Body fat (%)[a]	−0.016 [−0292; 0249]	−0.300 [−0579; −0002]
Fasting glucose (mg/dL)	−0.062 [−0358; 0231]	0.076 [−0204; 0356]
Insulin (μU/mL)	−0.239 [−0494; 0064][b]	−0.122 [−0435; 0215][c]
HOMA-IR	−0.167 [−0427; 0085]	−0.097 [−0406; 0212]
GPx1 activity (U/g Hb)	0.218 [−0064; 0475]	−0.129 [−0428; 0194]
SELENOP (ng/mL)	−0.350 [−0594; −0037] *	-
Plasma Se (μg/L)	0.010 [−0249; 0279]	−0.088 [−0371; 0208]
Erythrocyte Se (μg/L)	0.046 [−0254; 0343]	0.047 [−0262; 0372]
mRNA *GPX1* ($2^{-\Delta Ct}$)	0.126 [−0143; 0377]	−0.047 [−0380; 0259]
mRNA *SELENOP* ($2^{-\Delta Ct}$ x 10^3)	−0.264 [−0513; 0026]	−0.051 [−0352; 0252]
CRP (μg/mL)	0.085 [−0228; 0381]	−0.250 [−0536; 0059]
IL-6 (pg/mL)	0.112 [−0187; 0368]	−0.294 [−0560; 0001]
TNF-α (pg/mL)	−0.157 [−0444; 0138]	−0.265 [−0579; 0039]

Legend: [a]2 missing values, [b]7 missing values, [c]5 missing values. Legend: GPx= glutathione peroxidase; Se= selenium; SELENOP= selenoprotein P; IL-6= interleukin-6; CRP=C-reactive protein; TNF-α= tumor necrosis factor alpha. 95 % confidence interval in brackets [lower limit; upper limit]. *Bold indicates a significant p-value (< 0.05)

(HOMA-IR) was calculated using the equation: fasting glucose (mmol) x insulin (μU/mL)/22.5 [12].

2.4. Se biomarkers

Plasma and erythrocyte Se concentration were determined by inductively coupled plasma mass spectrometry (NexION® 2000 ICP Mass Spectrometer (ICP-MS), Perkin Elmer, USA), as previously described [13]. The reference material Seronorm Trace Elements Serum (SERO AS, Billingstad, Norway) was used for the quality control assessment. Found values were always in good agreement (t-test 95 %) with the target values. SELENOP plasma concentration was determined by enzyme-linked immunosorbent assay (ELISA) using a commercial kit (Abexxa, Ltd, Dallas/Fort Worth, TX, USA) on a microplate reader (Biotech Synergy H1, Biotek, Winooski, VT, USA). Erythrocyte GPx1 activity was determined according to the method of Paglia and Valentine [14] using a commercial kit (Ransel 505, Randox Laboratories, Crumlin, UK) in an automated biochemical analyzer and expressed in units per gram of hemoglobin (U/gHb). The reference values for plasma Se and erythrocyte Se were adopted as 60–120 μg/L and 90–190 μg/L, respectively [15].

2.5. GPX1 and SELENOP gene expression

Total RNA samples were extracted from peripheral blood mononuclear cells (PBMC) and cDNA synthesized by reverse transcription polymerase chain reaction as previously described [9]. The analysis of *GPX1* and *SELENOP* gene expression were performed by real-time quantitative PCR (qRT-PCR) on StepOne Plus equipment (Life Technologies, Foster City, CA, USA) using Taqman Gene Expression Assays specific for each gene. The glyceraldehyde phosphate dehydrogenase (GAPDH) was used as the reference gene.

2.6. miR-7-5p expression

The following experiments related to hsa-miR-7-5p expression were conducted at Exiqon Services, Vedbaek, Denmark, and were thoroughly described previously [16]. Total RNA was extracted from plasma samples using miRCURY RNA Isolation Kit–Biofluids, high-throughput bead-based protocol v.1 (Exiqon, Vedbaek, Denmark) in an automated 96-well format and cDNA synthetized using the miRCURY LNA Universal RT microRNA PCR Polyadenylation, and cDNA Synthesis Kit (Exiqon) according to the protocol described previously [17]. The relative levels of miRNA were measured using the comparative Ct method ($2^{-\Delta Ct}$) [18]. To normalize the results, the geometric mean of let-7i-5p and miR-30e-5p was adopted as the reference.

2.7. Statistical analyses

The variable distribution was evaluated using the Kolmogorov-Smirnov test and values were expressed as median and interquartile range. The correlation analysis between miR-7–5p and biochemical and anthropometric variables were performed using Spearman's test. Multiple logistic regression model was performed to evaluate variables predicting the high SELENOP concentration which was categorized based on the sample median: ≤78 μg/L = Low SELENOP; >78 μg/L = High SELENOP. Therefore, the Enter method was used and adjusted by miR-7–5p, statistically significant in the correlation, and age, body fat, TNF-α, fasting blood glucose, CRP, IL-6, according to possible interactions based on what was observed in the literature. Statistical analysis was performed using SPSS Statistics V23.0 software (IBM, IL, USA) and the p-value < 0.05 was considered statistically significant.

3. Results

The anthropometric and biochemical characteristics of the participants are shown in Table 1. Among the study participants, 18 % were diagnosed with T2D, and 19 % were using hypoglycemic medications. Moreover, clinical parameters demonstrate that more than 74 % of women have normoglycemic values according to Brazilian Diabetes guidelines [12]. Furthermore, plasma and erythrocyte Se concentration values were adequate according to the reference range [15], indicating that the participants did not present Se deficiency.

In order to verify the association between the miR-7-5p and clinical parameters, Se and inflammatory biomarkers, a correlation analysis were performed (Table 2). The results showed an inverse association between the miR-7-5p and SELENOP concentration (r = −0350; p = 0.018). No correlations were verified for the other parameters. Furthermore, it was also investigated the correlation between SELENOP concentration with clinical and biochemical parameters, but no significant association was observed.

To explore the association between the variables with the SELENOP concentration, we conducted a multiple logistic regression analysis adjusted for age, %BF, fasting glucose, CRP, TNF-α, IL-6, and miR-7-5p. The results demonstrated that the increase in age (OR = 1.21; 95 % CI = 1.06–1.40; p =0.007), lower percentage of body fat (OR = 0.74; 95 % CI= 0.57–0.95; p=0.019), and lower expression of miR-7–5p (OR = 0.99; 95 % CI = 0.983–0.998; p = 0.015) were significantly associated with higher SELENOP concentrations (>78 μg/L) (Table 3).

4. Discussion and conclusion

In this study, we demonstrated an inverse correlation between miR-7-5p and SELENOP levels. Furthermore, advanced age, lower percentage of body fat, and decreased expression of miR-7-5p were associated with high levels of SELENOP.

Although the miR-7-5p was not associated with plasma and erythrocyte Se levels, it was correlated with SELENOP concentration, whose protein translation seems to be inhibited by miR-7-5p [5]. It is important to note that dietary Se is absorbed in the gastrointestinal tract and predominantly transported via the bloodstream to the liver. In the liver, SELENOP is synthesized to regulate Se distribution systematically, ensuring that essential organs receive adequate amounts of this trace element [19,20]. Due to the capacity of miR-7-5p to bind to specific mRNA sequences and regulate gene expression, it plays a role in controlling protein levels and activity, which corresponds with the results

Table 3
Multiple Logistic Regression Model for predictors of SELENOP concentration above the median (>78 μg/L) in women with overweight/obesity.

	OR	95 % CI	p-value
Age (years)	1.214	1.055–1.397	**0.007**
Body fat (%)	0.737	0.571–0.952	**0.019**
CRP (μg/mL)	0.993	0.942–1.047	0.993
TNF- α (pg/mL)	0.286	0.069–1.182	0.084
IL-6 (pg/mL)	1.229	0.614–2.457	0.560
miR−7–5p ($2^{-\Delta Ct}$ x 10^3)	0.990	0.983–0.998	**0.015**
Fasting glucose (mg/dL)	1.006	0.967–1.046	0.766

Legend: Median was considered for the SELENOP cut-off value (≤78 μg/L = Low SELENOP; >78 μg/L = High SELENOP). CRP= C-Reactive Protein; TNF-α= tumor necrosis factor alpha; Interleukin-6= IL-6; OR= odds ratio; CI= confidence interval. Bold indicates a significant p-value (< 0.05).

obtained [21].

SELENOP is essential for regulating Se distribution to target tissues such as the nervous, endocrine and renal systems. Furthermore, this selenoprotein is involved in the homeostasis of this micronutrient, establishing a central role in its transport [19]. This selenoprotein is an indicator of selenium availability and is used as an accessible biomarker for assessing Se status through plasma sample measurements [22]. Studies have demonstrated that SELENOP concentration can be influenced by several factors, exhibiting variation according to gender. In contrast to previous findings, our study revealed that advanced age was associated with a higher level of SELENOP. However, it is important to highlight that our research did not include elderly women among the participants, which may have influenced the observed results [23].

Regarding the relationship between serum SELENOP concentration and body composition, previous studies have indicated that individuals with overweight exhibited higher values of this selenoprotein compared to individuals with obesity [24], whereas other findings showed that SELENOP correlates positively with visceral adiposity [25]. Thus, it is observed that various methods of assessing body composition may yield contrasting results in SELENOP regulation. Furthermore, other factors such as age, inflammation, genetic polymorphisms, glycemic disorders, among others, can also impact this concentration [23,24,26,27].

It is noted that selenoproteins are associated with miRNA in inflammatory diseases and cardiomyopathy, undergoing regulation beyond their target tissues [28]. A study in animals observed that miR-7-5p regulates the expression of the selenoprotein P gene in rats, possibly by repressing translation of the SELENOP transcript variant [29]. This finding aligns with our results, suggesting that miR-7-5p may be a significant regulator of SELENOP, indicating a potential impact on selenium nutritional status. However, further studies are needed to substantiate this regulation, as well as human studies to assess the impact of this miRNA modulation on physiological and pathophysiological aspects related to selenium.

Furthermore, another study conducted on patients undergoing bariatric surgery demonstrated that miR-7-5p was highly expressed in pineal gland tissue. Thus, this microRNA may be associated with the hormonal control of the thyroid and pineal gland, and consequently, it may be related to individual weight regulation [30].

miR-7–5p also demonstrates a potential role in the diagnosis of T2D and is associated with pancreatic B-cell growth, as suggested by *in silico* analyses indicating that miR-7–5p is related to the phosphorylation of proteins such as MAP kinase, AKT, and glycogen synthase kinase 3β, which are associated with insulin signaling. These proteins are found to be dysregulated in individuals with T2D or pre-diabetes. [6,31]. Other studies contribute to an increasing body of evidence regarding the role of miR-7–5p in the physiology of β cells, related to the pathophysiological process of diabetes, playing a potential role in the regulation of GLP-1-mediated insulin release [32]. Thus, the overexpression of miR-7–5p may lead to a reduction in the phosphorylation of proteins related to insulin function. [31,33,34].

Furthermore, protein kinase B (Akt) has been identified as a potential target of miR-7-5p, regulating the PI3K/Akt pathway in hepatocellular carcinoma as a possible tumor suppressor [31] and inhibiting the PI3K/Akt signaling pathway in intestinal epithelial cells [35]. This pathway plays a crucial role in the pathogenesis of type 2 diabetes and chronic diseases. Insulin activates the PI3K-Akt pathway, enabling the translocation of GLUT4 to the plasma membrane, which is crucial for insulin-regulated glucose transport [36,37].

The present study has some limitations. The small sample size which does not allow to make inferences for population. Additionally, another limitation is the scarcity of an extensive literature framework for discussing the findings, as there are not many studies in the literature addressing miR-7-5p.

However, the outcomes of this exploratory study will contribute with new data for Nutrimiromics areas regarding the interplay between miR-7-5p regulation, Se status, and inflammation, since there are few studies in the literature investigating this scenario. Therefore, this exploratory analysis serves as a crucial starting point for further research, providing support for new associations between microRNAs and micronutrients to bring new insights for future therapeutic strategies for mitigating metabolic complications in obesity.

In conclusion, this study presents a significant inverse association between plasma miR-7-5p expression and SELENOP concentration in overweight/obese women, suggesting that age and percentage of body fat are also positively associated, through different mechanisms that still need to be further elucidated, due to their actions on different targets that may be related to non-communicable chronic diseases, such as diabetes. Additionally, this study provides support for future research, with the possibility of corroborating the results of miR-7-5p related to selenium metabolism.

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Author statement

This statement confirms that this work is original and has not been published previously or is currently under consideration for publication elsewhere. All authors have reviewed and approved the final version of the manuscript and agreed to submit the manuscript to JTEMB.

CRediT authorship contribution statement

Higor Paiva de Mendonça Alves: Formal analysis, Writing, Statistical analysis. **Graziela Biude Silva Duarte:** Conceptualization, Methodology, Investigation. **Adriano Carlos de Souza Junior:** Formal analysis, Writing, Statistical analysis. **Leonam da Silva Pereira Batista:** Statistical analysis, Writing. **Marcelo Macedo Rogero:** Project administration, Supervision, Funding acquisition, Writing – review & editing.

Fernando Barbosa Jr: Validation, Formal analysis. **Silvia Maria Franciscato Cozzolino:** Project administration, Supervision, Funding acquisition, Writing – review & editing. **Raquel Costa Silva Dantas-Komatsu:** Formal analysis, Writing – original draft. **Karina Zaira Silva Marinho Costa:** Formal analysis, Statistical analysis, Writing. **Bruna Zavarize Reis:** Conceptualization, Methodology, Investigation.

Declaration of Competing Interest

The authors of this manuscript declare that there are no conflicts of interest.

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References

[1] M.F. Gregor, G.S. Hotamisligil, Inflammatory mechanisms in obesity, Annu. Rev. Immunol. 29 (2011) 415–445, https://doi.org/10.1146/annurev-immunol-031210-101322.
[2] G.B. Da Silva Duarte, B.Z. Reis, M.M. Rogero, Role of micronutrients zinc and selenium in inflammation and oxidative stress. Curr. Adv. Dev. Funct. Foods Modul. Inflamm. Oxidative Stress, Elsevier, 2022, pp. 181–188, https://doi.org/10.1016/B978-0-12-823482-2.00021-2.
[3] J.L.S. Donadio, G.B.S. Duarte, P. Borel, S.M.F. Cozzolino, M.M. Rogero, The influence of nutrigenetics on biomarkers of selenium nutritional status, Nutr. Rev. 79 (2021) 1259–1273, https://doi.org/10.1093/nutrit/nuaa136.
[4] B. Quintanilha, B. Reis, G. Duarte, S. Cozzolino, M. Rogero, Nutrimiromics: role of microRNAs and nutrition in modulating inflammation and chronic diseases, Nutrients 9 (2017) 1168, https://doi.org/10.3390/nu9111168.
[5] M. Tarek, M.L. Louka, E. Khairy, R. Ali-Labib, D. Zakaria Zaky, I.F. Montasser, Role of microRNA-7 and selenoprotein P in hepatocellular carcinoma, 101042831769837, Tumor Biol. 39 (2017), https://doi.org/10.1177/1010428317698372.
[6] L. Saeidi, S.Z. Shahrokhi, M. Sadatamini, M. Jafarzadeh, F. Kazerouni, Can circulating miR-7-1-5p, and miR-33a-5p be used as markers of T2D patients? Arch. Physiol. Biochem. 129 (2023) 771–777, https://doi.org/10.1080/13813455.2021.1871762.
[7] G. Langi, L. Szczerbinski, A. Kretowski, Meta-analysis of differential miRNA expression after bariatric surgery, J. Clin. Med. 8 (2019) 1220, https://doi.org/10.3390/jcm8081220.
[8] S.E. Stern, K. Williams, E. Ferrannini, R.A. DeFronzo, C. Bogardus, M.P. Stern, Identification of individuals with insulin resistance using routine clinical measurements, Diabetes 54 (2005) 333–339, https://doi.org/10.2337/diabetes.54.2.333.
[9] G.B.S. Duarte, B.Z. Reis, M.M. Rogero, E. Vargas-Mendez, F.B. Júnior, C. Cercato, S. M.F. Cozzolino, Consumption of Brazil nuts with high selenium levels increased inflammation biomarkers in obese women: a randomized controlled trial, Nutrition 63–64 (2019) 162–168, https://doi.org/10.1016/j.nut.2019.02.009.
[10] T.G. Lohman, Advances in Body Composition Assessment, Human Kinetics Publishers, Champaign, Ill, 1992.
[11] World Health Organization, Obesity: Preventing and Managing the Global Epidemic: Report of a WHO Consultation, World Health Organization, Geneva, 2000.
[12] A. Golbert, Diretrizes da Sociedade Brasileira de Diabetes (2019-2020), Editora Clannad, 2019.
[13] B.L. Batista, J.L. Rodrigues, J.A. Nunes, V.C. De Oliveira Souza, F. Barbosa, Exploiting dynamic reaction cell inductively coupled plasma mass spectrometry (DRC-ICP-MS) for sequential determination of trace elements in blood using a dilute-and-shoot procedure, Anal. Chim. Acta 639 (2009) 13–18, https://doi.org/10.1016/j.aca.2009.03.016.
[14] D.E. Paglia, W.N. Valentine, Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase, J. Lab. Clin. Med. 70 (1967) 158–169.
[15] P. Van Dael, H. Deelstra, Selenium, Int. J. Vitam. Nutr. Res. Int. Z. Vitam.-Ernahrungsforschung, J. Int. Vitaminol. Nutr. 63 (1993) 312–316.
[16] T. Blondal, S. Jensby Nielsen, A. Baker, D. Andreasen, P. Mouritzen, M. Wrang Teilum, I.K. Dahlsveen, Assessing sample and miRNA profile quality in serum and plasma or other biofluids, Methods 59 (2013) S1–S6, https://doi.org/10.1016/j.ymeth.2012.09.015.
[17] B.Z. Reis, G.B.S. Duarte, E. Vargas-Mendez, L.R.P. Ferreira, F. Barbosa, C. Cercato, M.M. Rogero, S.M.F. Cozzolino, Brazil nut intake increases circulating miR-454-3p and miR-584-5p in obese women, Nutr. Res. 67 (2019) 40–52, https://doi.org/10.1016/j.nutres.2019.05.004.
[18] T.D. Schmittgen, K.J. Livak, Analyzing real-time PCR data by the comparative CT method, Nat. Protoc. 3 (2008) 1101–1108, https://doi.org/10.1038/nprot.2008.73.
[19] L. Schomburg, Selenoprotein P – Selenium transport protein, enzyme and biomarker of selenium status, Free Radic. Biol. Med. 191 (2022) 150–163, https://doi.org/10.1016/j.freeradbiomed.2022.08.022.
[20] Y. Saito, Selenium transport mechanism via selenoprotein P—its physiological role and related diseases, Front. Nutr. 8 (2021) 685517, https://doi.org/10.3389/fnut.2021.685517.
[21] R. Szelenberger, M. Kacprzak, J. Saluk-Bijak, M. Zielinska, M. Bijak, Plasma microRNA as a novel diagnostic, Clin. Chim. Acta 499 (2019) 98–107, https://doi.org/10.1016/j.cca.2019.09.005.
[22] R.F. Burk, B.K. Norsworthy, K.E. Hill, A.K. Motley, D.W. Byrne, Effects of chemical form of selenium on plasma biomarkers in a high-dose human supplementation trial, Cancer Epidemiol. Biomark. Prev. 15 (2006) 804–810, https://doi.org/10.1158/1055-9965.EPI-05-0950.
[23] B. Lloyd, R.S. Lloyd, B.E. Clayton, Effect of smoking, alcohol, and other factors on the selenium status of a healthy population, J. Epidemiol. Community Health 37 (1983) 213–217, https://doi.org/10.1136/jech.37.3.213.
[24] A.A. Tinkov, O.P. Ajsuvakova, T. Filippini, J.-C. Zhou, X.G. Lei, E.R. Gatiatulina, B. Michalke, M.G. Skalnaya, M. Vinceti, M. Aschner, A.V. Skalny, Selenium and selenoproteins in adipose tissue physiology and obesity, Biomolecules 10 (2020) 658, https://doi.org/10.3390/biom10040658.
[25] H.Y. Choi, S.Y. Hwang, C.H. Lee, H.C. Hong, S.J. Yang, H.J. Yoo, J.A. Seo, S.G. Kim, N.H. Kim, S.H. Baik, D.S. Choi, K.M. Choi, Increased selenoprotein P levels in subjects with visceral obesity and nonalcoholic fatty liver disease, Diabetes Metab. J. 37 (2013) 63, https://doi.org/10.4093/dmj.2013.37.1.63.
[26] Z. Huang, A.H. Rose, P.R. Hoffmann, The role of selenium in inflammation and immunity: from molecular mechanisms to therapeutic opportunities, Antioxid. Redox Signal. 16 (2012) 705–743, https://doi.org/10.1089/ars.2011.4145.
[27] G.F. Combs, J.C. Watts, M.I. Jackson, L.K. Johnson, H. Zeng, A.J. Scheett, E. O. Uthus, L. Schomburg, A. Hoeg, C.S. Hoefig, C.D. Davis, J.A. Milner, Determinants of selenium status in healthy adults, Nutr. J. 10 (2011) 75, https://doi.org/10.1186/1475-2891-10-75.
[28] X. Huang, Y.-L. Dong, T. Li, W. Xiong, X. Zhang, P.-J. Wang, J.-Q. Huang, Dietary selenium regulates microRNAs in metabolic disease: recent progress, Nutrients 13 (2021) 1527, https://doi.org/10.3390/nu13051527.
[29] A.S.T. Dewing, R.H. Rueli, M.J. Robles, E.D. Nguyen-Wu, T. Zeyda, M.J. Berry, F. P. Bellinger, Expression and regulation of mouse selenoprotein P transcript variants differing in non-coding RNA, RNA Biol. 9 (2012) 1361–1369, https://doi.org/10.4161/rna.22290.
[30] S.L. Atkin, V. Ramachandran, N.A. Yousri, M. Benurwar, S.C. Simper, R. McKinlay, T.D. Adams, S.H. Najafi-Shoushtari, S.C. Hunt, Changes in blood microRNA expression and early metabolic responsiveness 21 days following bariatric surgery, Front. Endocrinol. 9 (2019) 773, https://doi.org/10.3389/fendo.2018.00773.
[31] M. Fernández-de Frutos, I. Galán-Chilet, L. Goedeke, B. Kim, V. Pardo-Marqués, A. Pérez-García, J.I. Herrero, C. Fernández-Hernando, J. Kim, C.M. Ramírez, MicroRNA 7 impairs insulin signaling and regulates A β Levels through posttranscriptional regulation of the insulin receptor substrate 2, insulin receptor, insulin-degrading enzyme, and liver X receptor pathway, Mol. Cell. Biol. 39 (2019) e00170-19, https://doi.org/10.1128/MCB.00170-19.
[32] A. Matarese, J. Gambardella, A. Lombardi, X. Wang, G. Santulli, miR-7 regulates GLP-1-mediated insulin release by targeting β-arrestin 1, Cells 9 (2020) 1621, https://doi.org/10.3390/cells9071621.
[33] L. Gan, S. Huang, Y. Hu, J. Zhang, X. Wang, Heat treatment reduced the expression of miR-7-5p to facilitate insulin-stimulated lactate secretion by targeting IRS2 in boar Sertoli cells, Theriogenology 180 (2022) 161–170, https://doi.org/10.1016/j.theriogenology.2021.12.029.
[34] Y.O. Nunez Lopez, A. Casu, Z. Kovacova, A.M. Petrilli, O. Sideleva, W.G. Tharp, R. E. Pratley, Coordinated regulation of gene expression and microRNA changes in adipose tissue and circulating extracellular vesicles in response to pioglitazone treatment in humans with type 2 diabetes, Front. Endocrinol. 13 (2022) 955593, https://doi.org/10.3389/fendo.2022.955593.
[35] F.C. Kalinowski, K.M. Giles, P.A. Candy, A. Ali, C. Ganda, M.R. Epis, R.J. Webster, P.J. Leedman, Regulation of epidermal growth factor receptor signaling and erlotinib sensitivity in head and neck cancer cells by miR-7, PLoS ONE 7 (2012) e47067, https://doi.org/10.1371/journal.pone.0047067.
[36] S. Gabbouj, S. Ryhänen, M. Marttinen, R. Wittrahm, M. Takalo, S. Kemppainen, H. Martiskainen, H. Tanila, A. Haapasalo, M. Hiltunen, T. Natunen, Altered insulin signaling in Alzheimer's disease brain – special emphasis on PI3K-Akt pathway, Front. Neurosci. 13 (2019) 629, https://doi.org/10.3389/fnins.2019.00629.
[37] B. Kim, E.L. Feldman, Insulin resistance in the nervous system, Trends Endocrinol. Metab. 23 (2012) 133–141, https://doi.org/10.1016/j.tem.2011.12.004.